Drugs Aging
DOI 10.1007/s40266-016-0429-3

ORIGINAL RESEARCH ARTICLE

Can a Multifaceted Intervention Including Motivational Interviewing Improve Medication Adherence, Quality of Life, and Mortality Rates in Older Patients Undergoing Coronary Artery Bypass Surgery? A Multicenter, Randomized Controlled Trial with 18-Month Follow-Up

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Abstract

Background Patients undergoing coronary artery bypass graft (CABG) surgery are required to take a complex regimen of medications for extended periods, and they may have negative outcomes because they struggle to adhere to this regimen. Designing effective interventions to promote medication adherence in this patient group is therefore important.

Objective The present study aimed to evaluate the long-term effects of a multifaceted intervention (psycho-education, motivational interviewing, and short message services) on medication adherence, quality of life (QoL), and mortality rates in older patients undergoing CABG surgery.

Methods Patients aged over 65 years from 12 centers were assigned to the intervention (EXP; $n = 144$) or treatment-as-usual (TAU; $n = 144$) groups using cluster randomization at center level. Medication adherence was evaluated using the Medication Adherence Rating Scale (MARS), pharmacy refill rate, and lipid profile; QoL was evaluated using Short Form-36. Data were collected at baseline; 3, 6, and 18 months after intervention. Survival status was followed up at 18 months. Multi-level regressions and survival analyses for hazard ratio (HR) were used for analyses.

Results Compared with patients who received TAU, the MARS, pharmacy refill rate, and lipid profile of patients in the EXP group improved 6 months after surgery ($p < 0.01$) and remained so 18 months after surgery ($p < 0.01$). QoL also increased among patients in the EXP group as compared with those who received TAU at 18 months post-surgery (physical component summary score $p = 0.02$; mental component summary score $p = 0.04$). HR in the EXP group compared with the TAU group was 0.38 ($p = 0.04$).

Conclusion The findings suggest that a multifaceted intervention can improve medication adherence in older patients undergoing CABG surgery, with these

Electronic supplementary material The online version of this article (doi:10.1007/s40266-016-0429-3) contains supplementary material, which is available to authorized users.

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Published online: 21 December 2016

improvements being maintained after 18 months. QoL and survival rates increased as a function of better medication adherence.
ClinicalTrials.gov NCT02109523.

Key Points

A multifaceted intervention including psycho-education, motivational interviewing, and short message services improved medication adherence among patients aged over 65 years who were undergoing coronary artery bypass graft (CABG) surgery.

The effects of the multifaceted intervention on medication adherence were maintained 18 months following the intervention.

Quality of life and survival rates improved as a consequence of increasing medication adherence.

1 Introduction

Coronary artery bypass graft (CABG) surgery is often considered to be the primary intervention for individuals with severe coronary artery disease and has been shown to increase quality of life (QoL) and life expectancy [1–3]. The mortality rate during CABG surgery has declined [4–8], including among older patients, even those aged 90 years or above [6, 7]. However, although CABG is a promising surgery for older patients with severe coronary artery disease, there are some reasons to suspect that older patients may have more negative outcomes after CABG surgery than younger patients [9, 10].

Patients undergoing CABG surgery are required to take a complex regimen of medications over a long period of time [9]. Therefore, one reason why older patients may have more negative outcomes is that they struggle to adhere to this regimen [10]. Some characteristics of the geriatric population, including hearing difficulties, impaired cognition, poor manual dexterity and vision, and low tolerance of the effects of drugs may result in low rates of adherence [11]. In addition, older patients undergoing CABG surgery share some of the factors that lead to noncompliance among younger patients, such as poor education about the importance and adverse effects of each medication, polypharmacy (the use of four or more medications), the need to take multiple doses each day, the cost of medication, and the incorrect use of medication [12]. Because medication adherence positively influences outcomes (e.g., decreases functional disability, morbidity, and mortality) [13, 14], it is important to design interventions that can improve medication adherence among older patients undergoing CABG surgery.

A meta-analysis of 33 randomized controlled trials of interventions designed to improve medication adherence among older patients [15] found that the interventions incorporating psycho-education, behavioral interventions, and interventions based on the theory of planned behavior significantly improved medication adherence (effect size, $d = 0.33$) and knowledge about medications ($d = 0.48$) relative to control conditions. However, the meta-analysis defined older patients in a relatively broad way (i.e., as those older than 60 years). Hence, their results may not generalize to older populations (i.e., those aged over 65 years); especially as age has been found to influence medication adherence among people with myocardial infarction [13]. Also, none of the primary studies focused on promoting medication adherence among older patients undergoing CABG surgery; therefore, more evidence is needed on interventions that can improve medication adherence for older patients undergoing CABG surgery.

Multifaceted interventions seem to be an appropriate way to promote medication adherence because many factors can simultaneously influence the behavior [16, 17]. For example, a prospective study found that medication counseling accompanied by planning increased medication adherence among patients with a mean age of 59 years undergoing CABG surgery [18]. However, given that older samples (e.g., those aged over 65 years) may have additional issues that prevent them from successfully adhering to medications (e.g., further impairments to hearing and cognition); it is possible that additional intervention components are needed to promote medication adherence among these patients. Therefore, the present research developed an intervention that consisted of psycho-education, motivational interviewing (MI) [19–21] accompanied by planning, and sending reminders via a short message service (SMS) [22] in an effort to increase medication adherence among patients aged over 65 years undergoing CABG surgery. The intervention also encouraged the patients' families to help because family members may influence medication adherence among patients undergoing CABG surgery [23], especially in Eastern cultures where family relationships are particularly valued [24].

In addition to identifying effective ways to promote medication adherence, it is also important to understand how and why interventions are effective—that is, to identify the underlying mechanisms. Multifaceted interventions likely change relevant cognitions and self-regulatory processes that, in turn, lead to changes in the outcomes of interest (namely, medication adherence). Based on extant research, it seems likely that patients'

intentions, behavioral automaticity, levels of action and coping planning, perceived behavioral control, self-monitoring, beliefs about medicines, and illness perceptions could all potentially mediate the effects of the intervention on outcomes (i.e., medication adherence, QoL, and mortality rate). Intentions reflect the direction and strength of a person's motivation to perform the relevant behavior (such as medication adherence in our study) [18]. Behavioral automaticity reflects whether a patient engages in a behavior (e.g., taking medication) relatively automatically; that is, quickly, easily, and without the need for conscious thought [25]. Action and coping planning reflect the extent to which patients have identified obstacles that may prevent them from engaging in a behavior and made plans specifying how they plan to deal with these; perceived behavioral control reflects how competent someone feels in their ability to perform a behavior [26]. Self-monitoring indicates whether someone regularly reflects on and monitors his/her behavior and/or the outcomes of their behavior [27, 28]. Beliefs about medicines refers to a patient's beliefs about the necessity and adverse effects of the medication they take [29], and illness perceptions indicate how a patient understands his/her illness [30]. A number of theoretical frameworks suggest that these social cognitions and self-regulatory processes affect the likelihood that a person will engage in a behavior [31–34]. Therefore, we considered that these factors could potentially mediate the impact of the multifaceted intervention on behavior (i.e., medication adherence). Moreover, because QoL and mortality rate are further outcomes of medication adherence [13, 14], medication adherence should mediate the effect of the intervention on QoL and mortality rates.

1.1 Objectives

The present study aimed to evaluate the long-term effects of a multifaceted intervention (including psycho-education, MI, and an SMS) on medication adherence (primary outcome), and QoL and mortality rates (secondary outcomes) in older patients undergoing CABG surgery. In addition, we measured a number of relevant social cognitions (e.g., strength of intentions to take medication) and self-regulatory processes (e.g., action and coping planning) as potential mediators of the effects of the intervention on medication adherence.

2 Methods

This trial was registered at ClinicalTrials.gov with the registration number NCT02109523.

2.1 Design and Study Population

The study adopted an open-label, researcher-blind, randomized controlled design, with two arms. Specifically, one arm received multifaceted intervention (see Sect. 2.3 for more details); another received treatment as usual (TAU) (see Sect. 2.5 for more details). Patients were recruited from multiple centers across Iran (five academic centers in Tehran, two in Qazvin and Ahvaz each, one in Semnan, Zanjan, and Tabriz each). Inclusion criteria were that patients (a) be aged 65 years or above, (b) had undergone CABG surgery, (c) had the ability to read and write Persian/Farsi, (d) provided informed consent to participate, and (e) had access to a mobile phone. Exclusion criteria were that patients (a) had already used Dosette boxes (or similar) to improve medication adherence, (b) were currently enrolled in another clinical trial, (c) had significant dysphasia, severe kidney disease (creatinine clearance <30 mL/min), oxygen-dependent chronic obstructive pulmonary disease, active hepatitis, significant hepatic failure, and/or a prior peptic ulcer (platelet count $<150 \times 10^9$), (d) were having concomitant surgery, (e) had a severe cognitive impairment [i.e., Mini Mental Status Examination (MMSE) score of <20], (f) had a myocardial infarction within 48 h of surgery, (g) were allergic to aspirin, (h) abused alcohol or narcotics, (i) reported ongoing bleeding, (j) had a terminal condition or were deemed unlikely to survive until 6-month follow-up, (k) were not being responsible for their own medication, and (l) the CABG was conducted as an emergency surgery. Patients with poor prognosis ($n = 2$) and those who had CABG as an emergency surgery ($n = 3$) were excluded to increase the likelihood that we were able to measure relevant outcomes at 18 months. Patients requiring emergency or urgent CABG are at higher risk than those undergoing CABG electively, and emergency CABG is typically carried out if serious complications develop after a heart attack (e.g., shock, life-threatening abnormalities of the heart rhythm, or rupture of heart tissues); thus, there is an increased risk of mortality among such patients [9].

Five trained general practitioners assessed each participant with respect to the aforementioned inclusion and exclusion criteria, after which all eligible patients were invited to participate in a group information session in a seminar room in their respective hospitals. In this session, the principal investigator and a surgeon explained the aims of the study and answered any questions that the patients had. Interested patients were then asked to sign a consent form and were assigned a unique study identification (ID) number. Following this, patients completed baseline measures ($n = 288$ patients completed this assessment). The measures were repeated at 6, 12, and 18 months after the intervention. Ethics approval was obtained from the review

committees of the different centers and partner institutions who approved the trial (QUMS.REC.1394.2). The study was conducted in accordance with the Ottawa Statement, the Helsinki Declaration, and Good Clinical Practice.

2.2 Randomization and Blinding

In order to minimize contamination and maximize the efficiency with which the intervention was delivered, centers were chosen as the units of randomization. Specifically, the centers were randomly assigned to either the intervention (EXP) or the TAU groups by an independent statistician following a 1:1 scheme using a computer-generated list of random numbers. Six centers were assigned to the EXP group and six centers were assigned to the TAU group. Figure 1 shows the flow of patients through the study.

The sample size needed to detect any effects of the intervention was calculated based on the primary outcome measure (self-reported medication adherence). It was estimated that 144 patients would be needed in each group to detect an effect (*difference*) = 1 score, with 90% power and a significance level of 5%, assuming a standard deviation of 1.9 in both groups, design effect of 1.8, and 5% loss at follow up. Exactly 144 patients were therefore allocated to each group as suggested by the sample size calculation.

All researchers responsible for measuring outcomes as well as statisticians were blinded to the group allocation. However, it was not possible for patients to be blind to group allocation because of the use of behavioral interventions. Therefore, objective measures of medication adherence such as total cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) concentrations were also evaluated, alongside self-reported rates of adherence to reduce the likelihood of demand effects.

2.3 Intervention

Patients in the EXP group received a multifaceted intervention that included (a) psycho-education, (b) MI, and (c) sending reminders via SMS. The intervention began the first week after the patients were discharged.

2.3.1 Psycho-Education

Patients in the EXP group participated in three weekly sessions accompanied by at least one family member with whom they had a close relationship (e.g., their son, daughter, spouse, brother or sister). The psycho-education component of the intervention was delivered by cardiovascular nurses. The contents and topics of psycho-education were discussed and preselected by cardiovascular nurses as well as cardiologists. The content of the psycho-education was the same for all patients and delivered orally. Each session lasted for 1 h and the main purpose was to provide information about coronary artery disease and ways of coping with the disease (e.g., the potential barriers to, and concerns about, coping with the disease). In addition, patients' experiences during previous visits, a list of previous medications and their effects and side effects, the reasons for previous medication non-adherence, as well as the reactions and communication between the family members about the patients' symptoms were discussed.

2.3.2 Motivational Interviewing (MI)

The patients in the EXP group attended five weekly sessions of MI that each lasted around 50 min. All sessions were held in a quiet, private, and comfortable setting inside the hospitals. The sessions were delivered by five trained and registered psychologists with experience (more than 100 h) in moderating MI sessions. These psychologists used several MI techniques that could potentially help the patients to increase their medication adherence, including open-ended questions, rolling with resistance, agenda setting, eliciting self-motivational statements, change talk, and affirmations. Following this, the psychologists highlighted factors that might interfere with the patients' plans to take their medication (also called *action planning*) and asked the patients to anticipate situations in which they might struggle to take their medication along with possible strategies that they might use to overcome these barriers (also called *coping planning*) [18]. At the end of the session, patients were asked to put the form on which they had written their plan(s) in a place that was easily visible and accessible for them. Detailed information on the procedure for the MI sessions is provided in the electronic supplementary material, Table S1.

2.3.3 Reminders via SMS

Four reminders were sent to patients on a monthly basis via text messages. The content of the messages differed each month as follows: (1) "The only way to improve your health is regular adherence to your medications;" (2) "Regular adherence to your medications will greatly help your recovery process and improve your health;" (3) "The most important factor for preventing a heart attack is that you take your medication regularly;" and (4) "Carefully consider which medication you take on a daily basis."

2.4 MI Integrity/Fidelity

In order to assess the quality and integrity of MI, all sessions were audiotaped. To evaluate integrity, the

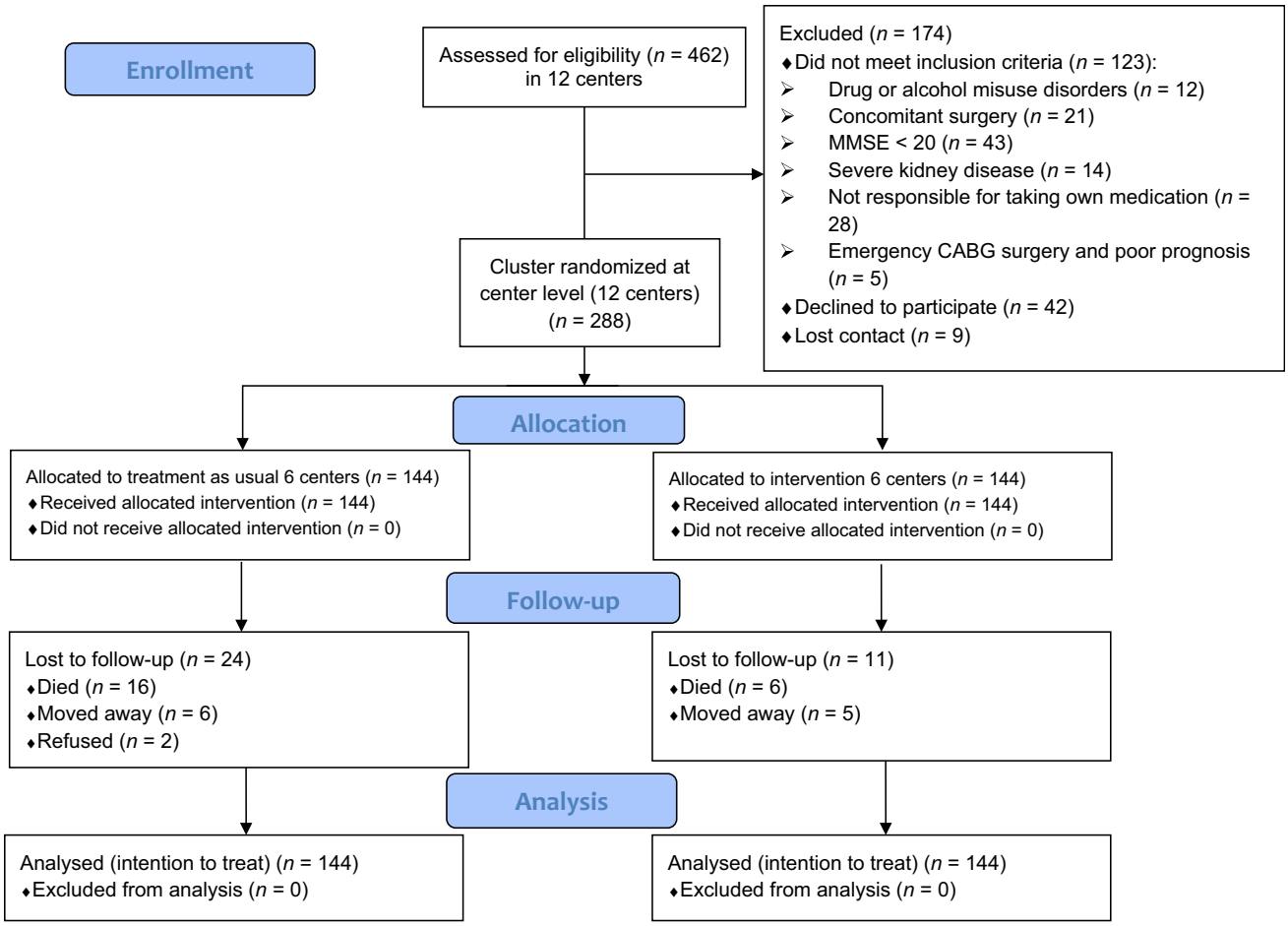

Fig. 1 Flow diagram for random assignment of patients in the study. *CABG* coronary artery bypass graft, *MMSE* Mini Mental Status Examination

Motivational Interviewing Treatment Integrity (MITI) scale 3.1.1 was used [35]. The MITI is a widely used measure of competences in MI. It normally makes use of a 20-min segment of each MI session and evaluates this segment based on global scores and behavior counts (two components of the MITI) to capture treatment fidelity. Twenty percent of the audiotaped sessions were selected randomly for evaluation by an independent/external coder. The global scores comprise five global ratings including evocation, collaboration, autonomy/support, direction, and empathy. The behavior counts include providing information, asking open- and closed-ended questions, providing simple and complex reflections, and making other statements categorized as MI adherent or not. In addition to the abovementioned components, five summary scores (i.e., each domain of the global ratings: evocation, collaboration, autonomy/support, direction, and empathy) were also computed to provide a more concise measure of competence.

Table S2 in the electronic supplementary material provides the global measures, behavior counts, and summary scores of the MITI. All of the facilitators who delivered the MI were competent, according to this measure. Specifically, the means of global measures were between 3.61 and 4.59, and the mean percentage of facilitators who were MI adherent was 93.12. Most means were slightly below competency, but above beginning proficiency.

2.5 Treatment as Usual

Patients allocated to the TAU group received the advice commonly given by surgeons on coronary artery disease and the CABG procedure, along with information on the importance of healthy diet and nutrition. Patients in the TAU group were further informed about the importance of medication adherence and encouraged to regularly take their medications, as well as being reminded of the negative consequences of nonadherence. Providing this information took approximately 30 min and took place in a room in the respective hospitals before the patients' discharge.

2.6 Outcomes

All outcomes were measured at baseline (before the intervention), and then 6, 12, and 18 months post-surgery. Detailed information on each of the measures is described below. The measures of intentions, action and coping planning, perceived behavioral control, and self-monitoring were based on similar measures used in previous research [18, 25–30], but were adapted so as to be relevant for Iranian patients undergoing CABG.

2.6.1 Medication Adherence Rating Scale

The Medication Adherence Rating Scale (MARS) is a short self-report scale measuring medication adherence that consists of five items which patients are asked to respond to on a 5-point Likert scale (from 1: always to 5: never) [36]. Scores range from 5 to 25 with higher scores indicating better medication adherence [18]. The Persian version of the MARS in the current study proved internally consistent (Cronbach's $\alpha = 0.89$).

2.6.2 Pharmacy Refill Rate

The pharmacy refill rate was defined as the number of days on which medications were dispensed to the patient during the study period, divided by the total number of days in the study period. This figure was then multiplied by 100 to give a percentage. All related information was collected monthly from 22 pharmacies in six cities and included the total number of pills prescribed along with the dates of each prescription. We assessed the cardiovascular medication adjusted for inpatient days and medication refills prior to enrollment date as well as information registered at 6 and 12 months' follow-up on change in prescriptions.

2.6.3 Lipid Profile

Serum lipid profiles were determined for all patients by taking 5 mL of venous blood after overnight fasting. Total cholesterol, triglycerides and high-density lipoprotein-cholesterol (HDL-C) concentrations were determined by the enzymatic colorimetric method. Low-density lipoprotein-cholesterol (LDL-C) concentrations, as well as serum total cholesterol, triglycerides and HDL-C concentrations were calculated using the Friedewald formula.

2.6.4 Intentions

Patients completed a short (5-item) questionnaire designed to measure their intentions to take medication, with items (e.g., "I intend to regularly take medicine in the future") being responded to on a 5-point Likert-type scale (from 1: completely disagree to 5: completely agree) [18]. The measure of intentions showed satisfactory internal consistency in this study (Cronbach's $\alpha = 0.90$).

2.6.5 Self-Report Behavioral Automaticity Index

The Self-Report Behavioral Automaticity Index (SRBAI) measures the extent to which a particular behavior (e.g., taking medication) is automatic for an individual [25]. The SRBAI consists of four statements that begin with "Behavior X is something…", followed by different descriptions, such as "I do automatically;" "I do without having to consciously remember;" "I do without thinking;" and "I start doing before I realize I am doing it." Patients are asked to rate the extent to which they agree with each of the statements on a 5-point Likert-type scale (from 1: disagree to 5: agree), and items were summed. The Persian version of the SRBAI was found to be highly reliable in this study (Cronbach's $\alpha = 0.91$).

2.6.6 Action and Coping Planning

Four items were used to measure action planning: "I have made a detailed plan regarding when/where/how often/how to take medication." Another four items were used to measure coping planning. Patients were provided with the stem "I have made a detailed plan regarding…" followed by four different endings: "…what to do if something interferes;" "…what to do if I forgot it;" "…how to motivate myself if I don't feel like it;" "…how to prevent being distracted" [26]. All items were rated on a 5-point Likert-type scale (1: completely disagree to 5: completely agree) and both the measures of action planning (Cronbach's $\alpha = 0.93$) and coping planning (Cronbach's $\alpha = 0.91$) proved internally consistent.

2.6.7 Perceived Behavioral Control

Perceived behavioral control (PBC) was measured with four items, to which patients responded on 5-point Likert-type scales. Items included "For me to take regular medication in the future is…" (1: difficult to 5: easy) and "It is up to me to take regular medication" (1: strongly disagree to 5: strongly agree) [26]. The measure of PBC proved internally consistent in this study (Cronbach's $\alpha = 0.93$).

2.6.8 Self-Monitoring

Self-monitoring was measured using three items on a scale that ranged from 1 (strongly disagree) to 5 (strongly agree). Each item consisted of a main sentence: "During the last month, I have consistently monitored…" with ending variations being "…when to take medications," "…how

often to take medications," and "…how to take medications" [27]. The internal consistency of self-monitoring in the present study was acceptable (Cronbach's $\alpha = 0.82$).

2.6.9 Beliefs About Medicines

Patients' beliefs about medication were measured using the Beliefs about Medicines Questionnaire (BMQ). Although the BMQ has specific and general sections, only the specific section, which is thought to be associated with adherence, was used in the present study [26]. The BMQ-specific reflects beliefs in two domains—necessity and concerns—and patients are asked to respond to statements reflecting each (e.g., "My health in the future will depend on my medication" [necessity] and "My medication disrupts my life" [concerns]) on a 5-point Likert-type scale (from 1: strongly disagree to 5: strongly agree). Scores on each domain can range from 5 to 25 with higher scores representing more worry about taking medicine. A study with an Iranian sample with diabetes used the Persian version of BMQ, and showed satisfactory psychometric properties [29]. The internal consistency of the BMQ-Necessity and BMQ-Concerns in the present study were Cronbach's $\alpha = 0.83$ and Cronbach's $\alpha = 0.85$, respectively.

2.6.10 Brief Illness Perception Questionnaire

The Brief Illness Perception Questionnaire (BIPQ) consists of nine items that assess illness perceptions in the following areas: identity, consequences, timeline, personal control, treatment control, concern, understanding, illness comprehensibility, and emotional representations [30]. Each item is rated on an 11-point Likert scale, where a higher score represents a higher level of illness perception. We used the total score (i.e., summing responses across each of the nine items), which represents the degree to which the illness is perceived as threatening or benign [30]. The internal consistency of the BIPQ in the present study was acceptable (Cronbach's $\alpha = 0.86$).

2.6.11 Health-Related Quality of Life: Short Form-36

The health-related QoL Short Form-36 (SF-36) includes 36 items, measuring both physical [physical component summary (PCS); sample item: "In general, would you say your health is…"] and mental (mental component summary [MCS]; sample item: "Have you felt calm and peaceful?") health. The scores were converted into a 0–100 scale, with higher scores indicating better QoL [37, 38]. The SF-36 has been translated into Persian and has been validated in a sample of Iranian hemodialysis patients showing satisfactory psychometric properties [39]. The internal consistencies of SF-36 subscales in the present study were acceptable and ranged from Cronbach's $\alpha = 0.74$ to Cronbach's $\alpha = 0.93$.

2.7 Statistical Analysis

Background information, clinical characteristics, and all outcome measures are described using means and standard deviations (SD) for continuous variables and frequency and/or percentages (%) for categorical variables. Multilevel linear mixed models were used to investigate the efficacy of the intervention taking into account the hierarchical nature of the data (i.e., that the patients were clustered in different centers) and repeated measures (i.e., that a number of outcomes were measured at several time points). Intention to treat (ITT) analysis was used, such that outcomes among all patients allocated to the groups were analyzed, whether they completed the intervention or not. We used three levels of analysis (repeated measures as the first, patients as the second, and centers as the third levels) with a restricted iterative generalized least square (RIGLS) estimation. This RIGLS computes unbiased estimates of the random parameters. In addition, we used univariate multilevel analyses to investigate the effects of potential confounding variables including age, education, family income, and body mass index. Confounding variables with a p value <0.20 were controlled for in the multivariate models. Consequently, each model was adjusted for the following potential confounding variables: age, sex, Charlson comorbidity index, and body mass index.

Potential mediators of the relationship between the intervention and medication adherence and between the intervention and QoL were examined using Sobel tests. Finally, survival analyses accounting for cluster effects of the hospitals were performed, with the cluster effects of centers being adjusted. All tests were two-tailed using a significance level of <0.05. The Benjamini and Hochberg false discovery rate was used to adjust p values for multiple comparisons where appropriate. Multilevel linear mixed modeling was conducted using MLwiN 2.27 software. Survival analyses were performed using the survival package in R (R Core Team 2014).

3 Results

After screening a total of 462 patients, 288 patients from 12 centers were eligible to participate in the study and the centers were randomly assigned to either the TAU or the EXP groups (Fig. 1). Thirty-five patients in the two groups dropped out during treatment. Table 1 summarizes the baseline and clinical characteristics of the two groups. The mean age of patients in the TAU group was 75.23 (SD

5.82) years and 74.32 (SD 5.26) years for the EXP group and nearly two-thirds of the patients were male (65.3% in TAU and 67.4% in EXP).

The descriptive statistics for medication adherence (including the MARS, objective pharmacy refill rate, and serum level of lipid profile), beliefs about medication, and QoL across the 18 months are reported in Table 2. Overall, patients in the EXP group showed better medication adherence after 6 months compared with patients in the TAU group, as indicated by the MARS (baseline: 7.68 ± 2.45 in EXP and 7.62 ± 2.76 in TAU; 6 months: 13.67 ± 2.80 in EXP and 7.69 in TAU), pharmacy refill rate (baseline: 62.30 ± 16.22 % in EXP and 61.41 ± 16.30 % in TAU; 6 months: 73.81 ± 18.56 % in EXP and 63.14 ± 17.21 % in TAU), HDL-C (baseline: 34.54 ± 9.89 % in EXP and 34.42 ± 9.74 % in TAU; 6 months: 42.74 ± 10.41 % in EXP and 34.18 ± 9.38% in TAU), and LDL-C (baseline: 113.75 ± 33.06 mg/dL in EXP and 115.20 ± 32.76 mg/dL in TAU; 6 months: 99.26 ± 36.75 mg/dL in EXP and 110.01 ± 35.78 mg/dL in TAU). Furthermore, medication adherence did not decrease after 18 months in the EXP group and patients in this group reported slightly better QoL, including PCS and MCS, than patients in the TAU group after 6 months.

After considering multicenter and other potential confounding factors and effects, the three-level multiple linear regression models showed that patients in the EXP group had better medication adherence after 6, 12, and 18 months compared with patients in the TAU group (see Table 3) as indicated by the MARS ($B = 3.97$ at 6 months, 3.83 at 12 months, and 4.24 at 18 months; $p < 0.01$), pharmacy refill rate ($B = 9.82$ % at 6 months, 10.64 % at 12 months, and 10.40 % at 18 months; $p < 0.01$), total cholesterol ($B = -7.40$ mg/dL at 6 months, -8.77 mg/dL at 12 months, and -8.60 mg/dL at 18 months; $p < 0.01$), LDL-C ($B = -12.45$ mg/dL at 6 months, -13.71 mg/dL at 12 months, and -13.59 mg/dL at 18 months; $p < 0.01$), HDL-C ($B = 8.41$ mg/dL at 6 months, 8.71 mg/dL at 12 months, and 8.87 mg/dL at 18 months; $p < 0.01$), and triglycerides ($B = -16.83$ mg/dL at 6 months, -18.86 mg/dL at 12 months, and -18.21 mg/dL at 18 months; $p < 0.01$).

About 11.1 % of the patients in the TAU group and 4.2 % of the patients in the EXP group had died before the end of follow-up (Fig. 2). When considering the loss at follow-up and drop-outs, a Gamma frailty survival model on the time of death showed that the crude hazard ratio (HR) in the EXP compared with the TAU group was 0.36 (95% CI 0.14–0.91, $p = 0.036$). After adjusting for the effects of age, sex, and number of diseased vessels, this HR continued to show a lower rate of death in the EXP group compared with the TAU group (adjusted HR 0.38; 95% CI 0.15–0.97, $p = 0.044$).

Tables S3 and S4 in the electronic supplementary material show the effects of intervention on intentions, perceived behavioral automaticity, self-monitoring, action and coping planning, beliefs about medicines, illness perceptions, and QoL. Patients in the EXP group reported better QoL than did patients in the TAU group after 18 months ($B = 1.77$ and $p = 0.02$ for PCS; $B = 1.68$ and $p = 0.04$ for MCS). The interactions between group and time tended to be significant such that patients in the EXP group (relative to those in the TAU group) tended to have more positive beliefs about taking medication, reported stronger intentions to take medication, and had perceptions of increased control over medication use. They were also more likely to have formed action and coping plans to support medication adherence and self-monitor their medication use; and reported that taking medication had become relatively automatic for them. Social cognitions and self-regulatory processes all mediated the effects of the intervention on medication adherence (See Table S5, electronic supplementary material). An additional mediation analysis showed that medication adherence mediated the effects of the intervention on outcomes such as QoL and survival rates.

4 Discussion

The present findings suggest that a multifaceted intervention with three components (psycho-education, MI, and SMS reminders) can improve medication adherence, QoL, and mortality rates among older patients undergoing CABG surgery. Specifically, patients who received the multifaceted intervention program (i.e., patients in the EXP group) showed increased MARS scores and higher pharmacy refill rates at 6 and 18 months after surgery. In contrast, MARS scores and pharmacy refill rates did not increase among patients who received conventional treatment and information (i.e., among patients in the TAU group). Other measures used to objectively assess medication adherence (including total cholesterol, HDL-C, TDL-C, and triglycerides) supported these conclusions and showed that patients in the EXP group were in better physiological health than patients in the TAU group in the 6–18 months after the intervention. In addition to medication adherence, patients who received the multifaceted intervention also reported better QoL and had a higher life expectancy compared with patients in the TAU group.

Previous studies have also reported beneficial effects of MI on medication adherence, albeit among different samples than those studied here, such as older people (aged 53–73 years) [40] and people with epilepsy [26]. Furthermore, previous studies attest to the efficacy of combining medical counseling with planning for promoting

Table 1 Comparison of clinical characteristics between the intervention (EXP) and treatment-as-usual (TAU) groups at baseline

	Treatment as usual ($n = 144$)	Intervention ($n = 144$)
Age, years; median (IQR)	76 (70–80)	75 (69–79)
Years of education; median (IQR)	4 (1–12)	4 (1–12)
Household income, Iranian rials[a]; median (IQR)	848.65 (453.40–1295.44)	893.06 (942.88–1286.88)
Body mass index, kg/m^2; mean ± SD	28.84 ± 5.57	28.64 ± 4.03
Marital status; *n* (%)		
Single	4 (2.8)	6 (4.2)
Married	90 (62.5)	92 (63.9)
Divorced/widowed	50 (34.7)	46 (31.9)
Sex; *n* (%)		
Male	94 (65.3)	97 (67.4)
Female	50 (34.7)	47 (32.6)
Ejection fraction; mean ± SD	45.23 ± 6.12	44.82 ± 7.02
Cross clamp time, min; mean ± SD	52.42 ± 25.81	54.21 ± 27.62
Cardiopulmonary bypass duration time, min; mean ± SD	96.68 ± 39.42	97.92 ± 40.35
Cardiac risk factors; *n* (%)		
Diabetes mellitus	55 (38.2)	52 (36.1)
Hypertension	107 (74.3)	110 (76.4)
Dyslipidemia	61 (42.4)	52 (36.1)
Myocardial infarction	86 (59.7)	90 (62.5)
Chronic lung disease	17 (11.8)	15 (10.4)
Prior cardiac surgery; *n* (%)	12 (8.3)	9 (6.2)
Current smoker; *n* (%)	21 (14.6)	18 (12.5)
No. of major vessels/branches bypassed; *n* (%)		
1 vessel	21 (14.6)	14 (9.7)
2 vessels	49 (34.0)	46 (31.9)
3 vessels	74 (51.4)	84 (58.3)
CCSC; *n* (%)		
I	12 (8.3)	10 (6.9)
II	24 (16.7)	15 (10.4)
III	48 (33.3)	51 (35.4)
IV	60 (41.7)	68 (47.2)
Charlson comorbidity index; *n* (%)		
0	40 (27.8)	36 (25.0)
1–3	79 (54.9)	81 (56.2)
≥4	25 (17.4)	27 (18.8)
Medications; *n* (%)		
Aspirin	135 (93.8)	132 (91.7)
Beta blockers	115 (79.9)	122 (84.7)
ACE inhibitors	98 (68.1)	90 (62.5)
Lipid-lowering drugs	105 (72.9)	109 (75.7)
Number of centers	6	6
Number of patients in each center	24	24

ACE angiotensin-converting enzyme, *CCSC* Canadian Cardiovascular Society Classification, *IQR* interquartile range, *SD* standard deviation

[a] 3500 rials = US$1 (April 2016 values)

medication adherence among patients undergoing CABG [18]. However, although a number of studies have shown the beneficial effects of such interventions, the current study combined the intervention components and, perhaps as a result, seemed to be even more effective in increasing medication adherence in older patients ($d = 2.13$ in the

Table 2 Descriptive statistics for all outcome measures across time in the intervention group (EXP) and the treatment-as-usual (TAU) group

Variable (normal range)	Group	Mean (SD)			
		Baseline	Month 6	Month 12	Month 18
BMQ-Necessity (5–25)	TAU	14.62 (3.22)	14.54 (3.30)	14.41 (2.42)	14.40 (3.07)
	EXP	14.37 (2.24)	18.69 (2.49)	18.64 (2.48)	18.53 (2.57)
BMQ-Concerns (5–25)	TAU	13.23 (4.05)	13.27 (4.0)	13.31 (4.27)	13.33 (4.12)
	EXP	12.92 (3.29)	7.81 (3.22)	6.02 (3.09)	4.78 (3.01)
Perceived behavioral control (1–5)	TAU	2.50 (0.93)	2.43 (0.98)	2.41 (0.99)	2.40 (0.93)
	EXP	2.49 (0.89)	3.00 (1.10)	2.98 (1.01)	2.99 (1.12)
Intention (1–5)	TAU	2.67 (0.65)	2.73 (0.69)	2.70 (0.70)	2.69 (0.69)
	EXP	2.72 (0.74)	3.44 (1.03)	3.41 (1.01)	3.42 (1.13)
Self-monitoring (1–5)	TAU	1.94 (0.40)	1.92 (0.51)	1.96 (0.75)	1.91 (0.82)
	EXP	2.06 (0.54)	2.65 (1.00)	2.67 (1.04)	2.66 (1.02)
Action planning (1–5)	TAU	1.93 (0.58)	1.190 (0.52)	1.88 (0.50)	1.86 (0.61)
	EXP	1.88 (0.57)	2.73 (1.13)	2.71 (1.30)	2.74 (1.29)
Coping planning (1–5)	TAU	1.68 (0.51)	1.64 (0.56)	1.61 (0.52)	1.62 (0.60)
	EXP	1.64 (0.54)	2.49 (1.11)	2.48 (1.19)	2.50 (1.26)
SRBAI (1–5)	TAU	1.91 (0.80)	1.87 (0.82)	1.86 (0.99)	1.83 (1.01)
	EXP	1.86 (0.87)	2.39 (0.94)	2.40 (0.98)	2.40 (1.14)
MARS (5–25)	TAU	7.62 (2.76)	7.69 (2.70)	7.71 (2.79)	7.63 (2.88)
	EXP	7.68 (2.45)	13.67 (2.80)	13.61 (2.82)	13.70 (2.75)
Illness perception (0–90)	TAU	36.43 (11.67)	35.57 (11.66)	36.63 (11.54)	36.67 (11.47)
	EXP	37.07 (11.78)	33.93 (12.53)	33.80 (12.72)	33.46 (10.17)
Pharmacy refill rate (0–100)	TAU	61.41 (16.30)	63.14 (17.21)	62.03 (18.77)	62.03 (18.77)
	EXP	62.30 (16.22)	73.81 (18.56)	73.48 (18.44)	73.24 (15.33)
Quality of life: PCS (0–100)	TAU	46.07 (11.66)	48.23 (11.70)	47.88 (12.05)	47.08 (10.10)
	EXP	46.88 (10.68)	50.04 (12.41)	50.29 (12.69)	49.93 (9.65)
Quality of life: MCS (0–100)	TAU	43.42 (12.76)	46.77 (11.41)	46.82 (11.33)	46.48 (10.35)
	EXP	44.92 (10.14)	49.39 (12.60)	49.76 (10.93)	49.69 (11.84)
Total cholesterol concentration (mg/dL)	TAU	182.90 (38.69)	180.76 (33.89)	180.71 (33.51)	180.53 (35.81)
	EXP	181.85 (39.00)	172.32 (40.71)	170.92 (32.12)	171 (32.00)
HDL-C (mg/dL)	TAU	34.42 (9.74)	34.18 (9.38)	33.88 (10.52)	33.52 (8.16)
	EXP	34.54 (9.89)	42.74 (10.41)	42.63 (11.29)	42.41 (9.31)
LDL-C (mg/dL)	TAU	115.20 (32.76)	110.01 (35.78)	113.32 (35.57)	114.51 (35.65)
	EXP	113.75 (33.06)	99.26 (36.75)	98.26 (27.32)	98.69 (27.41)
Triglycerides (mg/dL)	TAU	166.37 (66.60)	167.07 (65.99)	167.52 (55.43)	165.27 (65.21)
	EXP	167.61 (69.38)	151.55 (66.55)	150.13 (58.05)	149.33 (68.90)

BMQ Beliefs about Medicines Questionnaire, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *MARS* Medication Adherence Rating Scale, *MCS* Mental Component Summary, *PCS* Physical Component Summary, SRBAI Self-Report Behavioral Automaticity Index

present research; $d = 0.30$–1.02 in previous studies [18, 26, 40]). In short, the present findings support the effects of similar interventions conducted in other populations [21, 26, 40], such as patients with epilepsy, and show that MI and counseling can effectively enhance medication adherence in older individuals [41–44].

The present research also builds on previous studies by showing that a multifaceted intervention not only increases medication adherence but, as a result, can improve QoL and increase life expectancy in older patients receiving CABG. Interestingly, the effects on QoL were only observed at 18 months after surgery, compared with the changes in medication adherence that were observed at 6 months after surgery. However, this is to be expected given that both previous and the present research show that QoL is influenced by medication adherence and thus takes time to change [45–47]. In terms of the effects of the intervention on survival rates, previous studies have

Table 3 Three-level multiple linear regression models predicting medication adherence

Variable	MARS		Pharmacy refill rate		Total cholesterol		LDL-C		HDL-C		Triglycerides	
	B (SE)	*p* value	*B* (SE)	*p* value	*B* (SE)	*p* value	*B* (SE)	*p* value	*B* (SE)	*p* value	*B* (SE)	*p* value
Group (Ref: TAU)	0.30 (0.66)	0.36	2.37 (2.62)	0.26	−3.30 (7.25)	0.36	−3.01 (5.94)	0.35	15.52 (5.64)	**0.01**	−4.54 (9.73)	0.36
Time (Ref: baseline)												
6 months	0.38 (0.16)	**0.02**	1.81 (0.66)	**0.01**	−2.21 (1.34)	0.10	−2.22 (1.29)	0.09	0.12 (0.43)	0.38	−0.61 (1.79)	0.38
12 months	0.30 (0.14)	**0.045**	0.66 (0.46)	0.14	−2.26 (1.60)	0.15	−1.97 (1.31)	0.13	0.54 (0.40)	0.16	−1.21 (1.94)	0.33
18 months	0.05 (0.16)	0.38	0.91 (0.78)	0.20	−2.45 (1.60)	0.12	−1.79 (1.30)	0.16	0.92 (0.31)	**0.01**	−1.38 (1.86)	0.30
Group × time												
EXP vs TAU at 6 months	3.97 (0.22)	**<0.01**	9.82 (0.93)	**<0.01**	−7.40 (1.88)	**<0.01**	−12.45 (1.80)	**<0.01**	8.41 (0.60)	**<0.01**	−16.83 (2.52)	**<0.01**
EXP vs TAU at 12 months	3.83 (0.23)	**<0.01**	10.64 (0.95)	**<0.01**	−8.77 (1.92)	**<0.01**	−13.71 (1.93)	**<0.01**	8.71 (0.73)	**<0.01**	−18.86 (2.80)	**<0.01**
EXP vs TAU at 18 months	4.24 (0.26)	**<0.01**	10.40 (0.98)	**<0.01**	−8.60 (1.99)	**<0.01**	−13.59 (1.78)	**<0.01**	8.87 (0.60)	**<0.01**	−18.21 (2.70)	**<0.01**
Age	−0.19 (0.14)	0.17	−0.13 (0.13)	0.25	1.40 (1.41)	0.24	0.61 (1.23)	0.35	−0.92 (0.35)	**0.01**	0.46 (1.91)	0.39
Sex (Ref: females)	0.33 (0.47)	0.31	−8.32 (2.58)	**<0.01**	2.52 (1.63)	0.12	5.16 (3.68)	0.15	0.12 (0.10)	0.20	0.62 (0.86)	0.31
Charlson comorbidity index	−0.92 (0.65)	0.15	−1.69 (0.75)	**0.03**	9.59 (7.22)	0.17	−11.85 (6.91)	0.09	−6.64 (1.49)	**<0.01**	2.28 (0.98)	**0.03**
Body mass index	−0.06 (0.04)	0.16	−0.31 (0.61)	0.35	3.26 (1.26)	**0.01**	1.76 (4.01)	0.36	−0.35 (0.19)	0.07	8.37 (0.91)	**<0.01**
Intercept	11.14 (2.32)	**<0.01**	55.19 (8.66)	**<0.01**	164.84 (23.06)	**<0.01**	11.02 (2.26)	**<0.01**	15.21 (5.64)	**0.01**	187.83 (45.75)	**<0.01**
$\hat{\sigma}^2_{st}$ (patients)	14.97 (0.96)	**<0.01**	103.90 (13.19)	**<0.01**	46.70 (9.18)	**<0.01**	53.59 (8.41)	**<0.01**	93.12 (5.98)	**<0.01**	46.91 (15.61)	**<0.01**
$\hat{\sigma}^2_{sc}$ (centers)	3.52 (0.12)	**<0.01**	32.08 (11.64)	**0.01**	26.23 (8.58)	**<0.01**	37.21 (6.81)	**<0.01**	9.49 (3.88)	**0.02**	24.92 (16.10)	**0.12**

EXP intervention group, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *MARS* Medication Adherence Rating Scale, *Ref* reference group for comparison, *SE* standard error, *TAU* treatment as usual group, $\hat{\sigma}^2_{st}$ the variance at patient level, $\hat{\sigma}^2_{sc}$ the variance at center level

p values <0.05 are in bold

demonstrated that psycho-education and MI can reduce mortality in patients with different diseases [48–50], including coronary heart diseases. Our results echo such findings and further support the idea that the combination of psycho-education and MI can improve survival rates through medication adherence.

4.1 Strengths and Limitations

There are several strengths to our study. First, an 18-month follow-up without further intervention was used to investigate the long-term effects of the intervention on medication adherence and a number of health-related outcomes in patients undergoing CABG. As such, the findings provide important insights for clinicians with regards to the long-term effects of such interventions, not only on medication adherence but also on patients' overall health and QoL. Second, the present study included a variety of objective outcome measures to assess medication adherence and did not rely on self-report alone; therefore minimizing social desirability and reporting biases. Third, robust statistical analyses were conducted that accounted for potential confounding variables. By using multilevel linear mixed models, shared variance (e.g., accruing from recruiting patients from the same hospital) were minimized [51].

However, there are also some limitations that need to be considered when interpreting the findings. First, the effects of the intervention may not be generalizable to Western

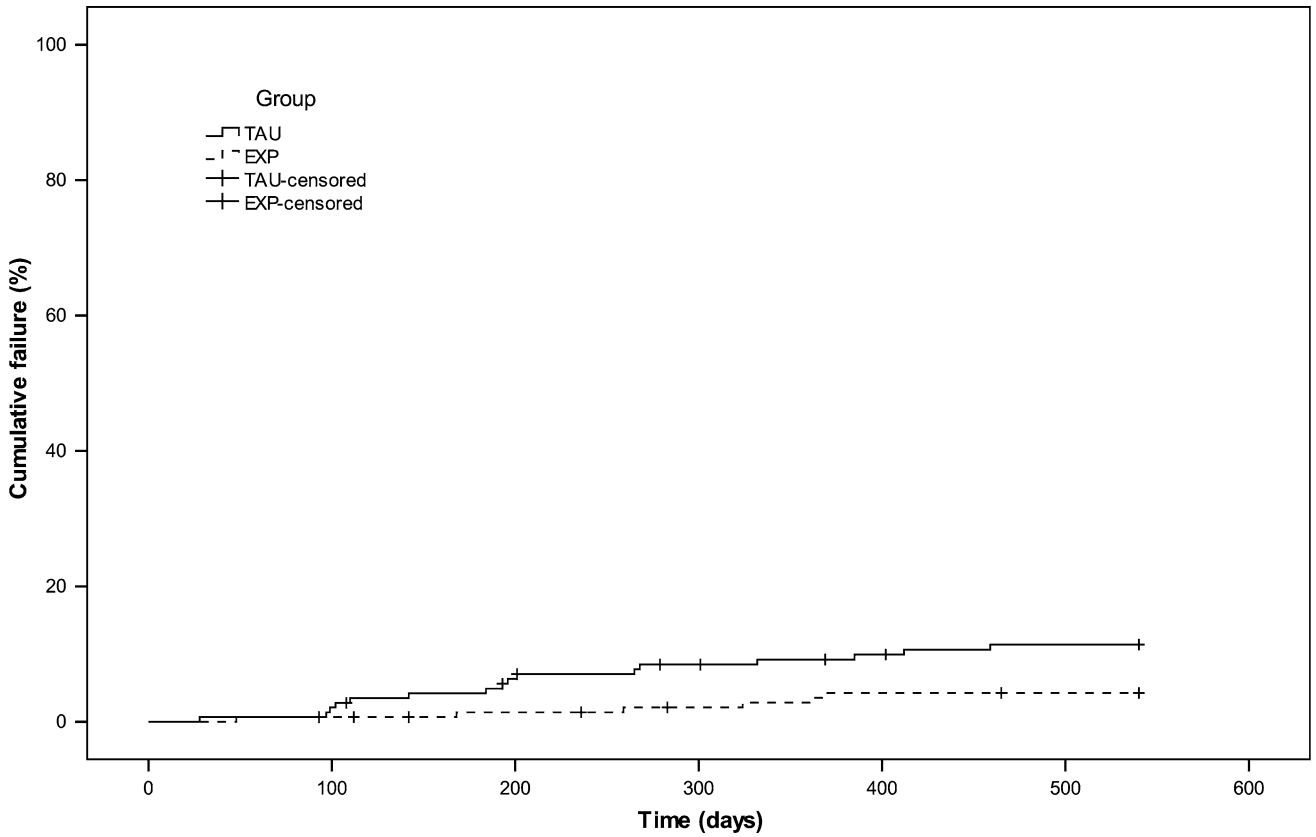

Fig. 2 Survival rates for patients in the multifaceted intervention group (EXP) and those in the treatment-as-usual group (TAU)

countries and cultures, particularly as the present research incorporated an element of family engagement. Unlike Western cultures that tend to emphasize individualism [52], family plays a crucial role for people with a Middle Eastern cultural background [53]. Second, patients with serious and/or specific health conditions (e.g., suffering from cognitive impairment or from a severe kidney disease) were excluded from the present research. Therefore, the findings may not generalize to other patients undergoing CABG who have additional health problems. Further studies are therefore warranted to investigate the effects of similar interventions in such groups. Third, because the present research developed and implemented a multifaceted intervention, the individual effects of each component cannot be separated. In other words, it is unclear which of the three components (psycho-education, MI, and SMS reminders) were effective in promoting medication adherence, and could potentially be used as individual components, or whether the outcomes were dependent on a joint effect. The larger effect size reported in the present research, relative to other studies that tested the effects of interventions that only incorporated one or some of these components, suggest that the multifaceted intervention was particularly beneficial, but factorial designs that directly compare interventions with different components are needed to corroborate this assertion. Lastly, the intervention used in the present research was relatively intensive and required a substantial time commitment from both the patients and those delivering the intervention. Although the findings were promising, further research could evaluate the cost effectiveness of the intervention relative to, for example, less complex interventions. Again, a factorial design would appear to be appropriate for this purpose.

5 Conclusion

The findings of the present study suggest that a multifaceted intervention consisting of psycho-educational, MI, and SMS reminders can promote medication adherence in older patients undergoing CABG, and that these effects are maintained 18 months after surgery. The increase in medication adherence as a function of the intervention also improved other health-related outcomes. Clinicians may therefore consider using multifaceted interventions to improve health and survival rates in older patients undergoing CABG.

Acknowledgements We thank all the patients and nurses as well as Mrs Mahdieh Pakpour who kindly helped us to collect data.

Compliance with Ethical Standards

Funding No sources of funding were used to assist in the conduct of this study or the preparation of this article.

Conflict of interest Chung-Ying Lin, Mehdi Yaseri, Amir H. Pakpour, Dan Malm, Anders Broström, Bengt Fridlund, Andrea Burri, and Thomas L. Webb declare that they have no conflicts of interest relevant to the content of this manuscript.

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